

**REMARKS**

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments, remarks and enclosures herewith.

**I. STATUS OF THE CLAIMS AND FORMAL MATTERS**

Claims 1-14 and 18-53 were pending in this application. Claims 1-13 and 27-51 have been withdrawn from consideration as allegedly being drawn to non-elected subject matter. Applicants reserve the right to pursue the withdrawn claims in this or future applications. Claims 14-25 and 52-53 have been cancelled without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is respectfully submitted that the claims, herewith and as originally presented, are patentably distinct over the art, and that those claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The remarks made herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, the amendments and remarks herewith are made simply for clarification and to round out the scope of protection to which Applicant is entitled.

**II. THE 35 U.S.C. § 102 REJECTIONS ARE OVERCOME**

Claims 14, 18-23, and 52 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Nestler *et al.* as evidenced by Parasrampuriah *et al.* and Monder *et al.*

Although the Applicants do not agree with the Office Action, in the interest of expediting prosecution, claims 14, 18-23, and 52 have been cancelled, rendering this rejection moot.

**III. THE 35 U.S.C. §103 REJECTIONS ARE OVERCOME**

Claims 24-25 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Nestler *et al.* as evidenced by Parasrampuriah *et al.* and Monder *et al.* and further in view of Kotelevtsev *et al.*

Although Applicants do not agree with the Office Action, in the interest of expediting prosecution, claims 24-25 have been cancelled.

Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Nestler *et al.* as evidenced by Parasrampuriah *et al.* and Monder *et al.* and further in view of Kotelevtsev *et al.* and further in view of Fruchart *et al.* Applicants respectfully traverse the rejection.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Although a teaching, suggestion, or motivation to combine is no longer rigidly required for a finding of obviousness, it remains the primary guarantor against a non-statutory hindsight analysis. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008). Further, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): “The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification.” For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicant’s disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Furthermore, The Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: “[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727.

Applying the law to the instant facts, the references relied upon by the Office Action do not disclose, suggest or enable Applicants’ invention.

The Office Action asserts that Fruchart *et al.* teach that PPAR $\alpha$  activators such as fibrates inhibit the development of atherosclerosis through their normolipidemic activities as well as through inhibition of vascular inflammation and thrombogenesis. The Office Action further contends that an ordinary skilled artisan would be motivated to use DHEA and PPAR $\alpha$  agonists in the treatment or reduction of atherosclerosis in order to produce an increased treatment outcome (See Office Action at page 9.)

Applicants respectfully disagree with the Office Action and submit that one of skill in the art would not be motivated to combine a PPAR $\alpha$  agonist with an 11 $\beta$ -HSD1 reductase inhibitor. The state of the art (See, for example, Berthiaume *et al.* and Berger *et al.*, submitted concurrently herewith) suggests that PPAR $\alpha$  agonists reduce 11 $\beta$ -HSD1 gene expression. In such a finding, it is implicit that there is no benefit in combining the two compounds. Based on the state of the art, the skilled artisan would predict that combining an 11 $\beta$ -HSD1 reductase inhibitor with a PPAR $\alpha$  agonist would produce no useful additional effect, since 11 $\beta$ -HSD1 reductase levels would be expected to be already reduced by the PPAR $\alpha$  agonist.

Applicants further submit that the invention recited in claim 26 of the present application is based on an unexpected finding, as discussed on page 52 lines 1-3 and page 60 lines 3-9 of the application as originally filed. Applicants demonstrated that in 11 $\beta$ -HSD1  $-/-$  mice, PPAR $\alpha$  expression is upregulated. This finding predicts synergism of 11 $\beta$ -HSD1 reductase inhibitors and PPAR $\alpha$  agonists, since suppression of 11 $\beta$ -HSD1 (in 11 $\beta$ -HSD1  $-/-$  mice) was found by the Applicants to enhance sensitivity to PPAR $\alpha$  agonists. In other words, the present application demonstrates the opposite of what is taught by what is known in the art. According to the present invention, when used with an 11 $\beta$ -HSD1 reductase inhibitor, a PPAR $\alpha$  agonist is expected to have a greater effect than when used alone. Thus, it was the Applicants' unexpected finding that prompted the combination of 11 $\beta$ -HSD1 and PPAR $\alpha$  in the presently claimed invention.

For the foregoing reasons, the references cited by the Examiner do not render the claimed subject matter *prima facie* obvious. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) are respectfully requested.

**REQUEST FOR INTERVIEW**

If any issue remains as an impediment to further examination and/or allowance, an interview with the is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

**CONCLUSION**

In view of the remarks and amendments herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the rejections of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP  
Attorneys for Applicants

By: 

Thomas J. Kowalski  
Reg. No. 32,147  
Deborah L. Lu  
Reg. No. 50,940  
Tel (212) 588-0800  
Fax (212) 588-0500